In the Claims:

The following listing of claims replaces all prior versions and listings of claims in the case.

1 – 17. (Canceled).

18. (Currently amended): A method of comparing protein expression in two or more populations of cells, said method comprising:

(a) contacting a first microarray comprising antibodies [[on]] coupled to a solid surface with a first cell lysate of a first cell population, thereby generating a first binding pattern, wherein the first cell lysate comprises antigens coupled to a first fluorescent dye;

(b) contacting either the first microarray of antibodies [[on]] coupled to the solid surface or a duplicate array comprising antibodies [[on]] coupled to a solid surface with a second cell lysate of a second cell population, thereby generating a second binding pattern, wherein the second cell lysate comprises antigens coupled to a second fluorescent dye; and

(c) comparing the first binding pattern with the second binding pattern to detect the presence of at least one protein that is differentially expressed in the first cell population with respect to the second cell population.

19 – 70. (Canceled)

71. (Previously presented): A method according to claim 18, wherein contacting a first microarray in step (a) is contacting a first microarray that comprises a collection of antibodies that recognize a set of mammalian antigens.

72. (Previously presented): A method according to claim 18, wherein contacting a first microarray in step (a) is contacting a first microarray that comprises 48 different antibody preparations.

73. (Previously presented): A method according to claim 72, wherein contacting a first microarray in step (a) is contacting a first microarray that comprises 90 different antibody preparations.

74. (Previously presented): A method according to claim 72, wherein contacting a first microarray in step (a) is contacting a first microarray that comprises a collection of antibodies that recognize a set of human antigens.

75. (Previously presented): A method according to claim 74, wherein contacting a first microarray in step (a) is contacting a first microarray that comprises a collection of antibodies that recognize a set of 1000 human antigens.

76. (Previously presented): A method according to claim 18, wherein contacting a first microarray in step (a) is contacting a first microarray that comprises a collection of antibodies that recognize a set of proteins expressed in a cell type.

77. (Previously presented): A method according to claim 75, wherein contacting a first microarray in step (a) is contacting a first microarray that comprises a collection of antibodies that recognize a set of proteins expressed in T cells.

78. (Previously presented): A method according to claim 76, wherein contacting a first microarray in step (a) is contacting a first microarray that comprises 90 different antibody preparations.

79. (Previously presented): A method according to claim 76, wherein contacting a first microarray in step (a) is contacting a first microarray that comprises a collection of antibodies that recognize a set of 1000 human antigens.

80. (Previously presented): A method according to claim 73, wherein contacting a first microarray in step (a) is contacting a first microarray that comprises a collection of antibodies that recognize a first set of antigens that are differentially expressed in a first disorder and a second set of antigens that are differentially expressed in a second disorder.

81. (Previously presented): A method according to claim 80, wherein contacting a first microarray in step (a) is contacting a first microarray that comprises 90 different antibody preparations.

82. (Previously presented): A method according to claim 80, wherein contacting a first microarray in step (a) is contacting a first microarray that comprises a collection of antibodies that recognize a set of 1000 human antigens.

83. (Canceled)

84. (Previously presented): A method according to claim 18, wherein contacting a first microarray in step (a) is contacting a first microarray that comprises a collection of antibodies that recognize a set of proteins of a pathogen.

85 – 87. (Canceled)

88. (Previously presented): A method according to claim 18, wherein in step (a) the first microarray is contacted with a first cell lysate comprising antigens coupled to a first cyanine dye and in step (b) either the first microarray or a duplicate array is contacted with a second cell lysate comprising antigens coupled to a second cyanine dye.

89. (Previously presented): A method according to claim 18, wherein in step (a) the first microarray is contacted with a first cell lysate comprising antigens coupled to a Cy3 dye and in step (b) either the first microarray or a duplicate array is contacted with a second cell lysate comprising antigens coupled to a Cy5 dye.

90. (Currently amended): A method of comparing protein expression in two samples, said method comprising:
    (a) labeling a first protein sample with a first fluorescent dye and a second protein sample with a second fluorescent dye;
    (b) removing unbound dye from the first sample and the second sample to generate a first labeled protein sample and a second labeled protein sample;
    (c) incubating the first labeled protein sample and the second labeled protein sample with a microarray comprising antibodies coupled to a surface thereof to generate a first binding pattern and a second binding pattern;

(d) ~~scanning the microarray to detect~~detecting the first binding pattern and the second binding pattern; and

(g) comparing the first binding pattern with the second binding pattern to detect the presence of at least one protein that is differentially expressed in the first sample with respect to the second sample.

91. (Previously presented): A method according to claim 90, wherein the labeling is labeling the first protein sample with a first cyanine dye and the second protein sample with a second cyanine dye.

92. (Previously presented): A method according to claim 90, wherein the labeling is labeling the first protein sample with Cy3 and the second protein sample with Cy5.

Remarks/Arguments

I. Status of the Claims:

Claims 18, 71 – 82, 84 and 88 – 92 stand rejected. Claims 18 and 90 are presently amended. No claims are presently cancelled. Claims 18, 71 – 82, 84 and 88 – 92 are pending on the case.

II. Issues Resolved from Previous Office Action:

Applicant acknowledges and appreciates the withdrawal of all previous rejections against the claims, as outlined on pages 2 and 8 of the instant Office action.

III. Rejections Under 35 USC §103:

A. Unlü, *et al.* in view of Blanc and Chu, *et al.*:

Claims 18, 71 and 88 – 92 stand rejected under 35 USC §103(a), as allegedly being obvious over Unlü, *et al.* (Electrophoresis, 1997, Vol. 18, pp. 2071 – 2077) (hereinafter "Unlü") in view of Bernard Blanc (Bulletin de la Societe de Chimie Biologiques, 1959, Vol. 41, pp. 891 – 899, English Abstract) (hereinafter "Blanc") and further in view of Chu, *et al.* (ACS Symposium Series, 1997, No. 657, Abstract only) (hereinafter "Chu"). The Examiner takes the position that Unlü describes the features of the instantly claimed methods but "is silent with respect to antibody utility in their 2-D electrophoresis procedures" and also with regard to "specifically teaching the use of an antibody array". The Examiner then asserts that the deficiencies of Unlü are remedied by the antibodies taught by Blanc and the microarrays taught by Chu. Applicant respectfully disagrees with these rejections for at least the following reasons.

Unlü describes a modified 2-D PAGE procedure in which two different protein samples are differentially labeled with fluorescent dyes and analyzed on a single polyacrylamide gel. Unlü states "[t]wo protein samples are pre-labeled with two cyanine dyes (Fig. 1), thus enabling one to run two different samples on the same gel in both dimensions" (Unlü, page 2071, Col. 2, 2nd paragraph).

In Unlü's method, the two differentially labeled samples are subjected to 2-D PAGE and the electrophoretic patterns are then visualized to detected changes in protein expression between the two samples. 2-D PAGE entails subjecting the samples to isoelectric focusing (IEF) to separate the samples in a first dimension based on charge, then using SDS-PAGE to separate constituent proteins in a second dimension based on size. In order for SDS-PAGE to work, proteins are contacted with SDS (sodium dodecyl sulfate), a strong ionic detergent, which denatures the proteins and allows their separation solely on the basis of mass, and not tertiary structure.

Blanc, on the other hand, relies on detecting the presence of specific proteins in electrophoresed samples by visualizing "precipitation arcs" caused by the diffusion of antibody-containing serum through the gel. In Blanc's method, a sample is first electrophoresed in one direction, followed by a second electrophoresis in a direction perpendicular to the first. Both electrophoretic steps are performed in agarose under non-denaturing conditions. The goal, as stated by Blanc, is to "make possible a better separation of antigen-antibody precipitation arcs, and thus easier differentiation of the corresponding constituents" (Blanc, Abstract, lines 4-5).

The Examiner argues that it would have been obvious to "use antibodies in electrophoresis procedures as taught by Blanc in the 2-D electrophoresis method of Unlü" (see Office action, page 4, 2nd paragraph). Applicant disagrees with this assertion and submits that there is no reasonable expectation that such a combination would be successful. Specifically, Applicant submits that because Unlü's method is performed in the presence of a denaturant, antigen-antibody complexes would not be expected to form between Unlü's labeled proteins and Blanc's antibodies.

Additionally, Blanc's method cannot be used to detect differentially expressed proteins between two different fluorescently-labeled samples in the same gel, since the Blanc's detection method requires the visualization of "arcs" of precipitated antibody-antigen complexes. Because the antigen-antibody complexes in Blanc precipitate, one cannot achieve the resolution required by Unlü's method.

More importantly, Blanc's method relies on the diffusion of an antibody through a gel matrix so that a precipitated complex can be formed between the antibody and proteins in the electrophoresed sample (see Blanc, Abstract, lines 2-3). Accordingly, Blanc's method will not work if the antibody is coupled to a solid support as instantly claimed.